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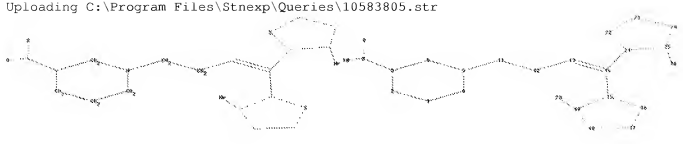

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chain nodes :
8  9  10  11  12  13  14  20  26
ring nodes :
1  2  3  4  5  6  15  16  17  18  19  21  22  23  24  25
chain bonds :
3-8  5-11  8-9  8-10  11-12  12-13  13-14  14-15  14-21  19-20  25-26
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  15-16  15-19  16-17  17-18  18-19  21-22  21-25  22-23
23-24  24-25
exact/norm bonds :
8-9  8-10  15-16  15-19  16-17  17-18  18-19  21-22  21-25  22-23  23-24  24-25

exact bonds :
1-2  1-6  2-3  3-4  3-8  4-5  5-6  5-11  11-12  12-13  13-14  14-15  14-21  19-20
25-26
isolated ring systems :
containing 1 : 15 : 21 :

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  8:CLASS  9:CLASS  10:CLASS  11:CLASS
12:CLASS  13:CLASS  14:CLASS  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom  20:CLASS
21:Atom
22:Atom  23:Atom  24:Atom  25:Atom  26:CLASS

L1      STRUCTURE UPLOADED


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Uploading C:\Program Files\Stnexp\Queries\10583805-HCl.str
Cl----H 1----2

chain nodes :
1  2
chain bonds :
1-2
exact bonds :
1-2

Match level :
1:CLASS  2:CLASS

L3      STRUCTURE UPLOADED


=> d his

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L1              STRUCTURE UPLOADED
L2           34 S L1 SSS FULL
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L3              STRUCTURE UPLOADED
L4           12 S L3 SSS FULL SUB=L2

     FILE 'CAPLUS' ENTERED AT 21:38:32 ON 15 AUG 2008
L5           61 S L4
L6           20 S L5 AND SPN/RL
L7       987000 S (POLYMORPH OR "XRD" OR "X-RAY" OR "X RAY")
L8            1 S L5 AND L7
L9           20 S L6 OR L8
L10           3 S US200!-583805/APPS
L11           1 S L9 AND L10
L12          19 S L9 NOT L10

=> d l11 bib abs

√L11  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2005:1355587  CAPLUS  Full-text
DN   144:74891
TI   Novel stable polymorphic forms of tiagabine hydrochloride
IN   Natarajan, Muthukumaran; Patel, Nileshkumar Sureshbhai; Bhatt, Mehul
     Chandrakatbhai; Kilaru, Srinivasu; Thennati, Rajamannar
PA   Sun Pharmaceutical Industries Limited, India
SO   PCT Int. Appl., 20 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        √APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------    --------
PI   WO 2005122698       A2     20051229    WO 2004-IN447           20041224
     WO 2005122698       A3     20060615
          W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
              CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
              GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
              LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
              NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
              SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
              AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
              EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
              RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
              MR, NE, SN, TD, TG
     IN 2003MU01210       A      20060616    IN 2003-MU1210          20031124
     US 20070066656       A1     20070322    US 2006-583805          20060622 <--
PRAI IN 2003-MU1210       A      20031124
     WO 2004-IN447        W      20041224
AB   Stable polymorphic forms III, IV and substantially amorphous forms of an
     anticonvulsant, tiagabine-HCl.  Thus, a monoacetonitrile solvate of tiagabine-
     HCl was prepared by the reaction of the drug hydrochloride with MeCN.  The
     solvate was characterized by x-ray diffraction.


=> d l12 tot bib abs hitstr

√L12  ANSWER 1 OF 19  CAPLUS  COPYRIGHT 2008 ACS on STN
PA   √Cephalon, Inc., USA
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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| | | | | | |
|---|---|---|---|---|---|
| PI | WO 2008021559 | A2 | 20080221 | WO 2007-US18413 | 20070817 |
| | US 20080051435 | A1 | 20080228 | US 2007-893524 | 20070816 |
| PRAI | US 2006-838661P | P | √20060818 | | |
| | US 2007-893524 | A | 20070816 | | |

√L12 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

SO Zhongguo Yiyao Gongye Zazhi √ (2006), 37(2), 75-77

√L12 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

SO Zhongguo Xinyao Zazhi √ (2005), 14(10), 1184-1187

√L12 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

√AU Anon.

SO Research Disclosure √ (2006), 505(May), P480 (No. 505017)

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | RD 505017 | | 20060510 | RD 2006-505017 | 20060510 |
| PRAI | RD 2006-505017 | | √20060510 | | |

√L12 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

SO Chemical Research in Chinese Universities √ (2006), 22(3), 351-355

√L12 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

PA √Nektar Therapeutics, USA

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2006062980 | A2 | 20060615 | WO 2005-US44133 | 20051207 |
| | WO 2006062980 | A3 | 20070208 | | |
| PRAI | US 2004-633953P | P | √20041207 | | |
| | US 2004-633991P | P | 20041207 | | |

√L12 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

SO √Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.

CODEN: CNXXEV

| | PATENT NO. | KIND | √DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | CN 1651426 | A | 20050810 | CN 2004-10089084 | 20041203 |
| PRAI | CN 2004-10089084 | | 20041203 | | |

√L12 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

PA √Ranbaxy Laboratories Limited, India

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2006013550 | A2 | 20060209 | WO 2005-IB52611 | 20050804 |
| | WO 2006013550 | A3 | 20060413 | | |
| | IN 2004DE01448 | A | 20060721 | IN 2004-DE1448 | 20040804 |
| | IN 2007DN01638 | A | 20070803 | IN 2007-DN1638 | 20070228 |
| PRAI | IN 2004-DE1448 | A | 20040804 | | |
| | WO 2005-IB52611 | W | √20050804 | | |

√L12 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

PA √Ranbaxy Laboratories Limited, India

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2005092886 | A1 | 20051006 | WO 2005-IB809 | √20050329 |
| | IN 2004DE00615 | A | 20060602 | IN 2004-DE615 | 20040329 |
| PRAI | IN 2004-DE615 | A | 20040329 | | |

√L12 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

SO Chinese Chemical Letters √ (2005), 16(9), 1205-1208

√L12 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

SO √Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given

| | PATENT NO. | KIND | √DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | CN 1554654 | A | 20041215 | CN 2003-10122778 | 20031224 |
| | CN 1651430 | A | 20050810 | CN 2004-10102052 | 20041215 |
| PRAI | CN 2003-10122778 | A | 20031224 | | |

√L12 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 20020099013 | A1 | 20020725 | US 2001-933708 | 20010822 |
| | US 20040087483 | A1 | 20040506 | US 2002-136433 | 20020502 |
| | US 7163918 | B2 | 20070116 | | |
| | US 20040063628 | A1 | 20040401 | US 2002-156527 | 20020529 |
| | US 7060708 | B2 | 20060613 | | |
| | IN 2003KN00775 | A | 20050204 | IN 2003-KN775 | 20030613 |
| | US 20070232529 | A1 | 20071004 | US 2004-923088 | 20040823 |
| | US 20060014697 | A1 | 20060119 | US 2005-89056 | 20050325 |
| | US 20070060500 | A1 | 20070315 | US 2006-392878 | 20060330 |
| | US 20080086016 | A1 | 20080410 | US 2007-745019 | 20070507 |
| | AU 2007203485 | A1 | 20070816 | AU 2007-203485 | 20070726 |
| PRAI | US 2000-247556P | P | 20001114 | | |

√AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or

more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.

√L12 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2002034237 | A1 | 20020502 | WO 2001-US26142 | 20010822 |
| | US 6716452 | B1 | 20040406 | US 2000-642820 | 20000822 |
| | CA 2420590 | A1 | 20020502 | CA 2001-2420590 | 20010822 |
| | AU 2001086599 | A | 20020506 | AU 2001-86599 | 20010822 |
| | EP 1311242 | A1 | 20030521 | EP 2001-966056 | 20010822 |
| | JP 2004523480 | T | 20040805 | JP 2002-537291 | 20010822 |
| | AU 2001286599 | B2 | 20070621 | AU 2001-286599 | 20010822 |
| | IN 2003KN00329 | A | 20041009 | IN 2003-KN329 | 20030320 |
| | IN 2007KN01482 | A | 20080801 | IN 2007-KN1482 | 20070425 |
| | US 20080086016 | A1 | 20080410 | US 2007-745019 | 20070507 |
| | AU 2007203485 | A1 | 20070816 | AU 2007-203485 | 20070726 |
| | KR 2008006024 | A | 20080115 | KR 2007-730727 | 20071228 |
| PRAI | US 2000-642820 | A | 20000822 | | |

√AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.

L12 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1998:13958 CAPLUS Full-text
DN 128:80001
OREF 128:15547a,15550a
TI Modified form of the tiagabine hydrochloride
IN Ahrndt, Preben; Petersen, Henning Borge; Chang, Vincent H.; Allen, Kimberly Ann; Chain, Michael H.
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9747619 | A1 | 19971218 | WO 1997-DK244 | 19970603 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU | | | | |
| | RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2257931 | A1 | 19971218 | CA 1997-2257931 | 19970603 |
| | CA 2257931 | C | 20061212 | | |
| | AU 9731653 | A | 19980107 | AU 1997-31653 | 19970603 |
| | AU 723267 | B2 | 20000824 | | |
| | EP 906309 | A1 | 19990407 | EP 1997-927006 | 19970603 |
| | EP 906309 | B1 | 20020904 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| | CN 1225094 | A | 19990804 | CN 1997-196341 | 19970603 |

| | | | | | |
|---|---|---|---|---|---|
| BR | 9709725 | A | 19990810 | BR 1997-9725 | 19970603 |
| HU | 9904035 | A2 | 20000528 | HU 1999-4035 | 19970603 |
| HU | 9904035 | A3 | 20000728 | | |
| JP | 2000511909 | T | 20000912 | JP 1998-501077 | 19970603 |
| IL | 127469 | A | 20010111 | IL 1997-127469 | 19970603 |
| RU | 2177478 | C2 | 20011227 | RU 1999-100703 | 19970603 |
| AT | 223405 | T | 20020915 | AT 1997-927006 | 19970603 |
| PT | 906309 | T | 20021231 | PT 1997-927006 | 19970603 |
| ES | 2181002 | T3 | 20030216 | ES 1997-927006 | 19970603 |
| CN | 1636565 | A | 20050713 | CN 2004-10092623 | 19970603 |
| CZ | 295578 | B6 | 20050817 | CZ 1998-4019 | 19970603 |
| PL | 190858 | B1 | 20060228 | PL 1997-330424 | 19970603 |
| US | 5958951 | A | 19990928 | US 1997-872380 | 19970610 |
| IN | 1997MA01240 | A | 20050304 | IN 1997-MA1240 | 19970610 |
| ZA | 9705266 | A | 19980204 | ZA 1997-5266 | 19970613 |
| NO | 9805809 | A | 19981211 | NO 1998-5809 | 19981211 |
| NO | 316889 | B1 | 20040614 | | |
| KR | 2000016580 | A | 20000325 | KR 1998-710175 | 19981211 |
| PRAI DK | 1996-661 | A | 19960614 | | |
| WO | 1997-DK244 | W | 19970603 | | |

AB R(-)-N-(4,4-di(3-methylthien-2-yl)but-3-enyl)nipecotic acid-HCl (tiagabine-HCl) in its pure and stable anhydrous form is described. Thus, tiagabine-HCl monohydrate (75 g) was dissolved in 613 mL water at 65°. The solution was filtered and 37 g concentrate HCl in 115 g water was added to the above solution, the while solution cooled and filtered and the precipitate was dried to give the anhydrous form of tiagabine_HCl.

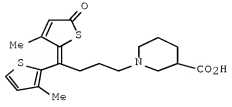
√L12 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1996:154157 CAPLUS Full-text
DN 124:260795
OREF 124:48311a,48314a
TI The synthesis of novel GABA uptake inhibitors. II. Synthesis of 5-hydroxytiagabine, a human metabolite of the GABA reuptake inhibitor tiagabine. [√Erratum to document cited in CA121:205185]
AU Andersen, Knud E.; Begtrup, Mikael; Chorghade, Mukund S.; Lee, Elaine C.; Lau, Jesper; Lundt, Behrend F.; Petersen, Hans; Soerensen, Per O.; Thoegersen, Henning
CS Den.
SO Tetrahedron (1996), 52(10), 3375
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier
DT Journal
LA English
AB The errors were not reflected in the abstract or the index entries.

L12 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1994:605185 CAPLUS Full-text
DN 121:205185
OREF 121:37357a,37360a
TI The synthesis of novel GABA uptake inhibitors. Part 2. Synthesis of 5-hydroxytiagabine, a human metabolite of the GABA reuptake inhibitor tiagabine
AU Andersen, Knud E.; Begtrup, Mikael; Chorghade, Mukund S.; Lee, Elaine C.; Lau, Jesper; Lundt, Behrend F.; Petersen, Hans; Soerensen, Per O.; Thoegersen, Henning
CS Novo Nordisk A/S, Nordisk Park, DK-2760, Den.
SO Tetrahedron (1994), 50(29), 8699-10

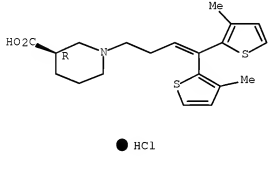
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
GI



I

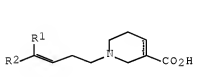
AB (R)-1-[4-(2,5-Dihydro-3-methyl-5-oxothien-2-ylidene)-4-(3-methyl-2-thienyl)butyl]-3-piperidinecarboxylic acid (5-hydroxytiagabine) (I) was prepared in 8 steps from 2-bromo-3-methylthiophene. Key steps are Grignard reactions, displacement of heteroarom. Cl with methoxy, and simultaneously demethylation and opening of a hydroxymethylcyclopropane with bromotrimethylsilane. A metalloporphyrin assisted hydroxylation of tiagabine also yielded the target metabolite. The structure of 5-hydroxytiagabine was confirmed by NMR-data including COSY, ROESY, HMQC and HMBC expts.
IT 145821-59-6, Tiagabine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydroxylation)
RN 145821-59-6 CAPLUS
CN 3-Piperidinecarboxylic acid, 1-[4,4-bis(3-methyl-2-thienyl)-3-buten-1-yl]-, hydrochloride (1:1), (3R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

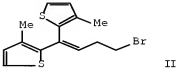


L12 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1993:472468 CAPLUS Full-text
DN 119:72468
OREF 119:13057a,13060a
TI The synthesis of novel GABA uptake inhibitors. 1. Elucidation of the structure-activity studies leading to the choice of (R)-1-[4,4-bis(3-methyl-2-thienyl)-3-butenyl]-3-piperidinecarboxylic acid (Tiagabine) as an anticonvulsant drug candidate
AU Andersen, Knud Erik; Braestrup, Claus; Groenwald, Frederik C.; Joergensen,

Anker S.; Nielsen, Erik B.; Sonnewald, Ursula; Soerensen, Per O.; Suzdak, Peter D.; Knutsen, Lars J. S.
CS Pharm. Div., Novo Nordisk A/S, Maaloev, DK 2760, Den.
SO Journal of Medicinal Chemistry (1993), 36(12), 1716-25
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI



I



II

AB A series of different synthetic approaches to novel GABA uptake inhibitors are described, leading to examples which are derivs. of nipecotic acid and guvacine, substituted at nitrogen by 4,4-diaryl-3-butenyl or 2-(diphenylmethoxy)ethyl moieties. Thus, diaryl/heteroarylbutenylpiperidi nes I (R1 = Ph, substituted Ph, 3-methyl-2-thienyl, 1-methyl-2-pyrrolyl, R2 = Ph, substituted Ph, 2-thienyl, 3-methyl-2-thienyl) were prepared Bromobis(methylthienyl)butene II reacted with Et 3-piperidinecarboxylate to give an intermediate [bis(methylthienyl)butenyl]piperidinecarboxylate which was hydrolyzed to give I (R1 = R2 = 3-methyl-2-thienyl). The in vitro value for inhibition of [3H]-GABA uptake in rat synaptosomes was determined for each compound It was found that the most potent examples are those having a substituent in an "ortho" position in one or both aromatic/heteroarom. groups. The majority of the compds. described are structurally related to tiagabine, (R)-1-[4,4-bis(3-methyl-2-theinyl)-3- butenyl]-3-piperidinecarboxylic acid hydrochloride (NNC 05-0328) and some of the reasoning behind the selection of this compound as a drug candidate is summarized.

√L12 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN -checked xrd
AN 1993:80815 CAPLUS Full-text
DN 118:80815
OREF 118:14217a,14220a
TI Crystalline tiagabine hydrochloride monohydrate, a method for its preparation and use as antiepileptic
IN Petersen, Henning; Nielsen, Peter; Cain, Michael; Patel, R. Subhash
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9217473 | A1 | 19921015 | WO 1992-DK93 | 19920323 |
| | W: AU, BG, CA, CS, FI, HU, JP, KR, NO, PL, RO, RU | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | CA 2107223 | A1 | 19921003 | CA 1992-2107223 | 19920323 |
| | CA 2107223 | C | 20050215 | | |
| | AU 9216415 | A | 19921102 | AU 1992-16415 | 19920323 |

| | | | | | |
|---|---|---|---|---|---|
| | AU 661483 | B2 | 19950727 | | |
| | EP 579681 | A1 | 19940126 | EP 1992-908325 | 19920323 |
| | EP 579681 | B1 | 19990602 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE | | | | |
| | JP 06506209 | T | 19940714 | JP 1992-507965 | 19920323 |
| | JP 3001975 | B2 | 20000124 | | |
| | AT 180781 | T | 19990615 | AT 1992-908325 | 19920323 |
| | ES 2134801 | T3 | 19991016 | ES 1992-908325 | 19920323 |
| | US 5354760 | A | 19941011 | US 1992-857038 | 19920324 |
| | IL 101358 | A | 19960804 | IL 1992-101358 | 19920324 |
| | ZA 9202297 | A | 19921230 | ZA 1992-2297 | 19920330 |
| | FI 110096 | B1 | 20021129 | FI 1993-4298 | 19930930 |
| | NO 9303524 | A | 19931001 | NO 1993-3524 | 19931001 |
| | NO 304113 | B1 | 19981026 | | |
| PRAI | DK 1991-582 | A | 19910402 | | |
| | WO 1992-DK93 | A | 19920323 | | |

AB Crystalline tiagabine hydrochloride monohydrate (I) is claimed. The use of I as antiepileptic agent is claimed (no data). Thus, Et tiagabinate was saponified and converted to the hydrochloride; this hydrochloride (174 g) was dissolved in water (5200 mL) and treated with concentrate HCl (154 mL) to give 99.7% pure I.

L12 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1987:515495 CAPLUS Full-text

DN 107:115495

OREF 107:18718h,18719a

TI Diheterocyclylbutenylamino acids as GABA uptake inhibitors

IN Groenvald, Frederik Christian; Braestrup, Claus

PA Novo Industri A/S, Den.

SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 8700171 | A1 | 19870115 | WO 1986-DK76 | 19860626 |
| | W: AU, DK, FI, JP, NO, US | | | | |
| | RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| | ZA 8604608 | A | 19870225 | ZA 1986-4608 | 19860620 |
| | CA 1284503 | C | 19910528 | CA 1986-512333 | 19860624 |
| | AU 8661336 | A | 19870130 | AU 1986-61336 | 19860626 |
| | AU 599326 | B2 | 19900719 | | |
| | EP 236342 | A1 | 19870916 | EP 1986-904114 | 19860626 |
| | EP 236342 | B1 | 19910911 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | JP 62503172 | T | 19871217 | JP 1986-503845 | 19860626 |
| | JP 07103116 | B | 19951108 | | |
| | AT 67196 | T | 19910915 | AT 1986-904114 | 19860626 |
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| | FI 89355 | B | 19930615 | | |
| | FI 89355 | C | 19930927 | | |
| | NO 8700781 | A | 19870225 | NO 1987-781 | 19870225 |
| | NO 168823 | B | 19911230 | | |
| | NO 168823 | C | 19920408 | | |
| | DK 8701008 | A | 19870226 | DK 1987-1008 | 19870226 |
| | DK 156398 | B | 19890814 | | |
| | DK 156398 | C | 19900108 | | |
| | US 5010090 | A | 19910423 | US 1988-254557 | 19881007 |

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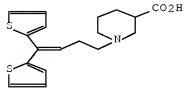
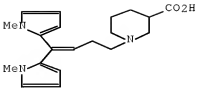
GI




II




III

AB R1R2C:CHCH2CH2R3 [I; R1, R2 = (un)substituted furanyl, thienyl, pyridyl, pyrrolyl; R3 = 3-carboxypiperidin-1-yl, 3-carboxy-1,2,5,6-tetrahydropyrid- 1-yl, 3-carboxymethylpyrrolidin-1-yl] and salts thereof were prepared as γ-aminobutyric acid uptake inhibitors. Cyclopropylmagnesium bromide reacted with di(2-thienyl) ketone to give di(2-thienyl)cyclopropyl carbinol, which reacted with HBr to give 4,4-di(2-thienyl)-3-butenyl bromide. This was aminated by Et nipecotate to give an intermediate which was saponified to afford dithienylbutenylnipecotic acid II. Dipyrrolylbutenylnipecotic acid III inhibited γ-aminobutyric acid uptake in Fjalland's screen with an IC50 of 60 nM. Capsules were prepared containing II 125, Mg stearate 2, and lactose 200 mg.

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STN INTERNATIONAL SESSION SUSPENDED AT 21:40:23 ON 15 AUG 2008